LA-UR-15-22709
Approved for public release; distribution is unlimited.

Title: X-ray structure determination using weak anomalous data

Author(s): Terwilliger, Thomas Charles
Hung, Li-Wei
Adams, Paul D.
Echols, Nathanial D
Grosse-Kunstleve, Ralf
Holton, James
Bunkoczi, Gabor
Read, Randy J.
Akey, David
Smith, Janet

Intended for: Asian Crystallographic Association Annual Meeting, 2015-12-05 (Kokata, India)
Recorded at a Phenix workshop at Rice University; also to be presented at IIT Bangalore Dec. 9 2015, Shanghai University Jan. 14-16 2016, Technion Univ, Haifa, Jan 4-6 2016.
Web

Issued: 2015-12-04 (rev.1)

Thomas C. Terwilliger[1], Gábor Bunkóczi[2], Nathaniel Echols[3], Ralf W. Grosse-Kunstleve[3], Li-Wei Hung[1], Janet Smith[4], David Akey[4], James Holton[3,5], Paul D. Adams[3], Randy J. Read[2]

[1]Los Alamos National Laboratory, Los Alamos NM 87545 USA
[2]Department of Haematology, University of Cambridge, Cambridge Institute for Medical Research, Wellcome Trust/MRC Building, Cambridge CB2 0XY, England
[3]Physical Biosciences Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720-8235, USA
[4]Life Sciences Institute, University of Michigan, Ann Arbor, MI 48109-2216, USA
[5]Department of Biochemistry and Biophysics, University of California, San Francisco, CA 94158

"X-ray structure determination using weak anomalous data"

A key challenge in the use of the SAD phasing method is the ability to carry out the process in cases where the anomalous signal-to-noise ratio is low. Here we describe new tools and algorithms for these challenging experiments.

We have developed a simple theoretical framework for describing measurements of anomalous differences and errors in measurement in a SAD experiment. Using this framework, we developed new tools for planning a SAD experiment, scaling SAD datasets, and estimating the useful anomalous signal in a SAD dataset. The *phenix.plan_sad_experiment* tool helps a user identify the overall I/sigI needed in a dataset to find the substructure and obtain useful phase information based on a database of solved and unsolved SAD datasets. The *phenix.scale_and_merge* tool scales unmerged SAD data from one or more crystals using local scaling and optimizes the anomalous signal by identifying the systematic differences among datasets. The *phenix.anomalous_signal* tool estimates the anomalous signal in a dataset and estimates the probability that the dataset can be solved and the

likely figure of merit of phasing. These tools will be demonstrated using SAD datasets available from the PDB and from a recent highly redundant S-SAD data collection.

We have also developed a likelihood-based method for determining the sub-structure of anomalously-scattering atoms in a macromolecular crystal. The approach uses log-likelihood gradient maps and likelihood scoring to complete potential solutions to the substructure found using anomalous difference Patterson methods. The likelihood-based method can solve very challenging substructures and is now available in combination with other enhancements in SAD phasing, including the use of a partial model or an electron density map in iteration of the search for anomalously-scattering atoms. Additionally, automated testing of alternative values of parameters, including the method used to identify solvent in density modification, the number of cycles of density modification, applying or not applying anisotropy correction, and choice of resolution used for sub-structure determination, is carried out. The results of using these approaches with a large set of SAD datasets will be presented.